

### **Remarks**

This paper is being provided in Response to the March 21, 2006 Office Action for the above-referenced application. Claims 1-7, 9-17, 19-21, 28, 43, 44, 46, and 162-165 are currently pending. Claim 1 has been amended. Applicant respectfully submits that the amendments to the claims are supported by the originally filed application.

Applicant has maintained in this application the claims withdrawn by the Examiner. Upon allowance of a linking claim, Applicant respectfully submits that any claims depending for or otherwise including all of the limitations of an allowable linking claim should be subsequently rejoined in the present application and allowed.

### **Rejection under 35 U.S.C. § 132(a), New Matter**

On July 20, 2005, Applicant submitted a Petition to Claim Priority Under 37 C.F.R. § 1.78, along with an Amendment to the Specification reflecting the same. The Petition to Claim Priority has not yet been reviewed and granted. It is respectfully submitted that the language cited will not be new matter if the petition is granted.

### **The Claimed Invention**

The claimed invention discloses an apparatus comprising at least one suspended beam, wherein the beam encases at least one sealed microfluidic channel, and the surface of the microfluidic channel is treated to bind to or react with an analyte. The apparatus may further comprise a device for measuring change in a mechanical property of the beam.

### **Rejections under 35 U.S.C. § 102(b)**

#### ***Boisseau***

Claims 1, 2, 162 and 165 are rejected under 35 U.S.C. § 102(b) as being anticipated by Boisseau. Specifically, the Examiner states that Boisseau discloses an apparatus for detecting an analyte comprising a suspended beam comprising a microfluidic channel (motility scanner #50) and connected to at least one mechanically stable support (support #16) wherein the channel has at least one chemical species (e.g., diluents e.g. Hepes) that reacts with the analyte (e.g., sperm); and further comprising a detector for measuring a change in the beam e.g. CCD; and wherein the beam is in a controlled environment i.e. portable housing.

Boisseau is directed towards a device for measuring the motion of sperm, bacteria, and other particles as viewed in an optical microscope. The Examiner identifies a motility scanner (#50) as a microfluidic channel. However, Applicant notes that this element (#50) denotes a specimen holder. Applicant therefore further responds under the assumption that the Examiner meant to characterize the specimen holder (#50) as a microfluidic channel. Boisseau describes the specimen channel to have dimensions of 5 cm x 2 mm x 0.2 mm (*see* Col. 5, lines 39-45). Boisseau therefore discloses a device that is a conventional flow cell, but is not a microfluidic chamber. The specimen channel of Boisseau has a volume of 0.02 ml, which is roughly five orders of magnitude ( $\sim 10^5$ ) larger than the sub-nanoliter scale of microfluidics. As defined by [http://whatis.techtarget.com/definition/0,,sid9\\_gic526632,00.html](http://whatis.techtarget.com/definition/0,,sid9_gic526632,00.html), "[m]icrofluidics is the science of designing, manufacturing, and formulating devices and processes that deal with volumes of fluid on the order of nanoliters or picoliters. The devices themselves have dimensions ranging from millimeters down to micrometers. Microfluidics hardware requires construction and design that differs from macroscale hardware. It is not generally possible to scale conventional devices down and then expect them to work in microfluidics applications. When the dimensions of a device or system reach a certain size as the scale becomes smaller, the particles of fluid, or particles suspended in the fluid, become comparable in size with the apparatus itself. This dramatically alters system behavior. Capillary action changes the way in which fluids pass through microscale-diameter tubes, as compared with macroscale channels. In addition, there are unknown factors involved, especially concerning microscale heat transfer and mass transfer..."

Applicant respectfully submits that one of ordinary skill in the art would understand the term "microfluidics" to deal with volumes of fluids appropriately defined by the order of nanoliters or picoliters. Applicant further submits that one of ordinary skill in the art would understand the term 'microfluidic channel' to have a depth and/or height in the range of between about a fraction of a micron and about 100 microns. *See* Declaration under 37 C.F.R. § 1.132 of Scott Manalis, Ph. D., submitted herewith. As stated above, the specimen channel of Boisseau has a volume of 0.02 ml, which is roughly five orders of magnitude ( $\sim 10^5$ ) larger than the microfluidic channels as presently claimed.

The Examiner further suggests that the channel in Boisseau has at least one chemical species (Hepes) that reacts with the analyte (e.g., sperm). The Examiner states (or reiterates from Applicant's last response) that the Hepes of Boisseau "serves as the media into which the sperm is suspended." The Examiner states therefore, that the Hepes "reacts" with the sperm by suspending the sperm in the media. However, as Applicant stated previously, Hepes is a chemical buffer solution consisting of various salts dissolved in water. It does not *react* with the sperm. A reaction is defined by *a chemical transformation or change*. The suspension of sperm within the Hepes is not a reaction. The Hepes buffer is used to dilute the sperm to a desired concentration. Hepes is known to one of ordinary skill in the art as a buffer solution that does not have any specific binding affinity or reactivity with sperm.

Regarding claim 2, the Examiner states that the instant claim recites an intended use of the apparatus but does not further define or further limit the structure of the apparatus. Applicant respectfully disagrees. The term to "treat" is defined as to act upon with some agent especially to improve or alter. *See, e.g., <http://www.m-w.com/dictionary/treat>*. Applicant respectfully submits that claim 2 appropriately recites the apparatus of claim 1 with the further limitation wherein the microfluidic channel is treated with a capture ligand that binds to the analyte.

Claims 2, 162, and 165 depend from independent claim 1. Applicant respectfully submits that Boisseau does not disclose, teach or suggest all of the elements of the presently claimed invention. Therefore, Applicant respectfully requests that these rejections be reconsidered and withdrawn.

### ***Pinkel***

Claims 1-2 and 161-162 are rejected under 35 U.S.C. § 102(b) as being anticipated by Pinkel. Specifically, the Examiner states that Pinkel discloses an apparatus for detecting analyte comprising a suspended beam comprising a microfluidic channel (specimen slide with grooves or channel formed between slide and coverslip) and connected to at least one mechanically stable support (specimen holder) wherein the channel has at least one chemical species that reacts with the analyte; further comprising a detector for measuring a change in the beam e.g. CCD; wherein the beam is in a controlled environment e.g. arms for positioning slide; and wherein the chemical species is a capture ligand that binds analyte.

Pinkel does not disclose, teach or suggest a microfluidic chamber or channel. For example, in Col. 9, lines 16-19 of Pinkel, the illumination system is designed to image regions 0.5-1 cm<sup>2</sup> in area. A liquid drop covering this area and sandwiched between a glass slide and a cover plate would typically be in the range of microliters, which is at least three orders of magnitude (~1000X larger) than the boundaries of microfluidics. Applicant respectfully submits that one of ordinary skill in the art would understand the term “microfluidics” to deal with volumes of fluids appropriately defined by the order of nanoliters or picoliters. Applicant further submits that one of ordinary skill in the art would understand the term ‘microfluidic channel’ to have a depth and/or height in the range of between about a fraction of a micron and about 100 microns. *See* Declaration under 37 C.F.R. § 1.132 of Scott Manalis, Ph. D., submitted herewith. As explained above, Pinkel does not disclose, teach or suggest the invention as presently claimed.

Regarding claim 2, the Examiner states that the instant claim recites an intended use of the apparatus but does not further define or further limit the structure of the apparatus. Applicant respectfully disagrees. The term to “treat” is defined as to act upon with some agent especially to improve or alter. *See, e.g.,* <http://www.m-w.com/dictionary/treat>. Applicant respectfully submits that claim 2 appropriately recites the apparatus of claim 1 with the further limitation wherein the microfluidic channel is treated with a capture ligand that binds to the analyte.

Applicant respectfully requests that these rejections be reconsidered and withdrawn.

#### **Rejection under 35 U.S.C. § 102(a)**

##### ***Savran***

Claims 1, 2, 43-44 and 162 are rejected under 35 U.S.C. § 102(a) as being anticipated by Savran. Specifically, the Examiner states that Savran discloses an apparatus comprising at least one beam (cantilever) suspended and connected to at least one mechanically stable support wherein the beam contains microfluidic channels (trenches) having chemical species (gold) for analyte reaction; wherein the channels have a depth of between 100 and 3000 nm; wherein the channels have a thickness of between 100 and 1200 nm; and wherein the apparatus is within a controlled environment.

Savran describes two adjacent suspended beams with channels used to detect bending induced by biomolecular interactions of molecules. However, Savran does not disclose, teach or

suggest *sealed* microfluidic channels on a suspended beam. The sealed microfluidic channels of the present invention provide numerous advantages, including but not limited to, higher flow volumes and immunity from evaporation, leakage and unwanted cross-contamination.

Applicant also submits that Savran discloses a cantilever beam *inserted into* a microfluidic channel. Applicant has amended claim 1 to replace the term “contains” with the term “encases,” thereby clarifying the presently claimed invention. The microfluidic channel is not encased within the cantilever beam, as is recited by the presently claimed invention. The technique disclosed by Savran of inserting a cantilever beam into a microfluidic chamber has been disclosed in a number of publications and patent applications. All of these schemes previously disclosed have the limitation that the cantilever must move against the viscous damping forces of the surrounding liquid. These damping forces dramatically reduce the sensitivity of the measurement.

Therefore, Applicant respectfully submits that Savran does not disclose, teach or suggest all of the elements of the presently claimed invention.

Regarding claim 2, the Examiner states that the instant claim recites an intended use of the apparatus but does not further define or further limit the structure of the apparatus. Applicant respectfully disagrees. The term to “treat” is defined as to act upon with some agent especially to improve or alter. *See, e.g.,* <http://www.m-w.com/dictionary/treat>. Applicant respectfully submits that claim 2 appropriately recites the apparatus of claim 1 with the further limitation wherein the microfluidic channel is treated with a capture ligand that binds to the analyte.

Applicant respectfully requests that these rejections be reconsidered and withdrawn.

### **Rejections under 35 U.S.C. § 102(e)**

#### ***Fritz***

Claims 1-2, 28, 43-44 and 161-162 are rejected under 35 U.S.C. § 102(e) as being anticipated by Fritz. Applicant respectfully notes that claim 161 has been cancelled. With respect to claims 1-2, 28, 43-44 and 162, the Examiner states that Fritz discloses an apparatus comprising at least one beam (cantilever, 710<sub>1</sub>, Fig. 7) suspended and connected to at least one mechanically stable support (mounting surface, 720, Fig. 7) wherein the beam contains microfluidic channels (sensing surface, 100<sub>1</sub>, Fig. 7 with sample containing region, 105 as illustrated in Fig. 1) having chemical species (probe molecules, 115, Fig. 1) for analyte reaction

(¶ 28-31).

Like Savran above, Applicant submits that Fritz discloses a cantilever beam *inserted into* a microfluidic channel. The microfluidic channel of Fritz is not encased within the cantilever beam. The technique of Fritz has the limitation that the cantilever must move against the viscous damping forces of the surrounding liquid. These damping forces dramatically reduce the sensitivity of the measurement. Applicant has amended claim 1 to replace the term “contains” with the term “encases,” thereby clarifying the presently claimed invention. Applicants respectfully submit that Fritz does not disclose, teach or suggest all of the elements of the presently claimed invention. Therefore, Applicants request that these rejections be reconsidered and withdrawn.

### ***Manalis***

Claims 1-7, 19, 28, 43-44, 161 and 162 are rejected under 35 U.S.C. § 102(e) as being anticipated by Manalis. Applicant respectfully notes that claim 161 has been cancelled. With respect to claims 1-7, 19, 28, 43-44 and 162, Applicant filed a Petition to Claim Priority under 35 C.F.R. § 1.78 to Manalis (U.S. Patent Application Publication No. 2004/0038426, filed 2 January, 2003) on July 20, 2005. Accordingly, Applicant respectfully submits that upon the granting of the above-noted petition, Manalis will no longer be a proper 102(e) reference. Applicant respectfully requests that this rejection be withdrawn.

### ***Geli***

Claims 1-7, 9-14, 43-44 and 163-164 are rejected under 35 U.S.C. § 102(e) as being anticipated by Geli. Specifically, the Examiner states that Geli discloses an apparatus comprising at least one beam (cantilever, 13, Fig. 3-4) wherein the beam contains microfluidic channels i.e., made of porous material (¶ 270) and connected to microchannels (claims 15) having chemical species for analyte reaction i.e., functional groups and capture molecules (¶ 270-272). The Examiner further explains that Geli teaches measurement of cantilever "suspended" beams because Geli discloses a portion of a cantilever which flexes and/or resonates.

Like Fritz, Geli discloses a cantilever beam *inserted into* a microfluidic channel. The microfluidic channel is not encased within the cantilever beam, as is disclosed by the present

invention. The technique disclosed by Geli of inserting a cantilever beam into a microfluidic chamber has been disclosed in a number of publications and patent applications. All of these schemes previously disclosed have the limitation that the cantilever must move against the viscous damping forces of the surrounding liquid. These damping forces dramatically reduce the sensitivity of the measurement. Applicant has amended claim 1 to replace the term "contains" with the term "encases," thereby clarifying the presently claimed invention. Applicant respectfully submits that Geli does not disclose, teach or suggest the elements of the present invention. Therefore, Applicant requests that these rejections be reconsidered and withdrawn.

### **Rejection under 35 U.S.C. § 103(a)**

#### ***Geli in view of Kley***

Claims 15-17, 19-21, 28, 46 and 162 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Geli in view of Kley. The Examiner proposes that it would have been obvious to one of ordinary skill in the art to apply various elements of Kley to the apparatus of Geli. Applicant respectfully disagrees. As stated above, Geli discloses a cantilever beam *inserted into* a microfluidic channel. The microfluidic channel is not contained within the cantilever beam, as is disclosed by the present invention. The technique disclosed by Geli of inserting a cantilever beam into a microfluidic chamber has been disclosed in a number of publications and patent applications. All of these schemes previously disclosed have the limitation that the cantilever must move against the viscous damping forces of the surrounding liquid. These damping forces dramatically reduce the sensitivity of the measurement. Applicants respectfully submit that Geli does not disclose, teach or suggest the claimed elements of the present invention as amended.

Applicant respectfully submits that Kley does not overcome the above-noted deficiencies of Geli with respect to Applicant's presently claim invention. Kley does not disclose, teach or suggest analyte detection (or any equivalent thereof). Kley discloses an atomic force microscope for inspection and modification of sample surfaces. An instrument based in part on this technology is sold by Rave LLC ([http://www.ravelle.com/photomask\\_repair.html](http://www.ravelle.com/photomask_repair.html)). This instrument uses atomic force microscopy ("AFM") cantilevers wherein one cantilever is used to inspect photomasks and the other cantilever is used to repair the defects. The purpose of the vacuum environment referred to in Kley (*see* Col. 35, lines 35-42) is to increase the accuracy of the scanning probe microscopes ("SPM") measurements and surface modifications, which is

unrelated to analyte detection.

As stated above, the present invention is an apparatus comprising at least one suspended beam, wherein the beam encases at least one microfluidic channel, and the surface of the microfluidic channel is treated to bind to or react with an analyte. The apparatus may further comprise a device for measuring change in a mechanical property of the beam. Applicant respectfully submits that neither Geli nor Kley, taken alone or in combination, disclose, teach or suggest these elements of the present invention. Applicant further submits that it would not be obvious to one of ordinary skill in the art to combine the references, as Geli does not disclose at least one microfluidic channel encased within a suspended beam and further teaches away from the present invention, and Kley does not discuss or suggest analyte detection. Therefore, Applicant respectfully requests that the Examiner reconsider and withdraw these pending rejections.

#### **Double Patenting**

##### ***Fritz, 10/201,333***

The provisional rejection of Claims 1-7, 9-17, 19-21, 28, 43-44 under the judicially created doctrine of obviousness-type double patenting over claims 1-23 and 30-33 of co-pending Patent Application No. 10/201,333 has been addressed by the filing of a Terminal Disclaimer (Terminal Disclaimer 1) herewith. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

##### ***Manalis, 10/336,549***

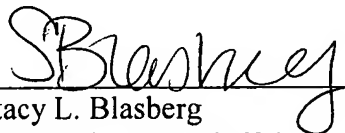
The provisional rejection of Claims 1-7, 9-17, 19-21, 28, 43-44 under the judicially created doctrine of obviousness-type double patenting over claims 13-24 of co-pending Patent Application No. 10/336,549 has been addressed by the filing of a Terminal Disclaimer (Terminal Disclaimer 2) herewith. Accordingly, Applicant respectfully requests that this rejection be withdrawn.




Based on the above, Applicant respectfully requests that the Examiner reconsider and withdraw all outstanding rejections and objections. Favorable consideration and allowance are earnestly solicited. Should there be any questions after reviewing this paper, the Examiner is invited to contact the undersigned at 617-248-4054.

Please charge any necessary fees or credit any overpayments to our Deposit Account No. 03-1721.

Respectfully submitted,

  
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